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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/544,934	04/07/2000	Henrik Stender	35853.1	2473

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EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/544,934	STENDER ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

1. The previous final rejection is withdrawn, since it was mailed prior to the completion by Applicant of the requirements for the CPA application. Now that the CPA requirements have been fulfilled, this action is applied to the invention. This action will be made FINAL, because all the current claims could have been finally rejected based upon the grounds and art of record.

Continued Prosecution Application

2. The request filed on December 21, 2001, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/544,934 is acceptable and a CPA has been established. An action on the CPA follows.

Election/Restrictions

3. The previous restriction is carried over into this case, in the absence of any indication by Applicant that a shift is desired. Therefore, claims 43-50 and 58-60, drawn to specific sequences, are examined only insofar as they include one of the 10 elected sequences. They are included in the prior art rejections for the sake of compact prosecution, but prior to any allowance, the non-elected sequences will be required to be cancelled.

Sequence Rules

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR

1.821 through 1.825 for the reasons of record. Applicant is requested to comply with the sequence rules and to correct the sequence errors shown in the attached Raw Sequence Listing Error Report processed August 7, 2002.

Priority

5. The application now complies with the priority requirements and priority to October 3, 1997 is now granted.

Claim Rejections - 35 USC § 102

6. The rejection under 35 U.S.C. 102(b) under Stender is withdrawn in view of the priority claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 37-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over being unpatentable over one of Shah et al (U.S. Patent 5, 521,300) or Hogan et al (U.S. Patent 5,541,308) or Britschgi et al (U.S. Patent 5,726,021), any one of the previous in view of Hyldig-Nielsen et al (WO 95/32305).

Shah teaches probe for detecting a mycobacterial target sequence which probes comprise SEQ ID NO: 8 (see column 93, SEQ ID NO: 72) and SEQ ID NO: 85 (see column 77, SEQ ID NO: 35).

Hogan teaches probe for detecting a mycobacterial target sequence which probes comprise SEQ ID NO: 25 (see column 24, line 21) and SEQ ID NO: 34 (see column 18, line 20).

Britschgi teaches probe for detecting a mycobacterial target sequence which probes comprise SEQ ID NO: 123 (see column 71, SEQ ID NO: 83).

Neither Shah, Hogan or Britschgi teach the use of PNA backbones in oligonucleotide probes.

Hyldig-Nielsen teaches the use of PNA backbones, including a backbone of the formula of claims 42, 54, (see page 17 of Hyldig-Nielsen) in probes for the detection of microorganisms using 16S rRNA base compositions (abstract). Hyldig-Nielsen expressly teaches that Z is NH, R2 is H, R3 is H, R4 is H, X and Y are O and Q is a nucleobase on page 17. Hyldig-Nielsen further teaches the use of labels and solid phase hybridization systems (page 3 and page 17). Hyldig-Nielsen further teaches the use of kits, which incorporate solid phase capture systems (page 45).

With regard to claims 52-54, Hyldig Nielsen expressly teaches amino acid linkers such as His or Asp (see page 17, line 10).

With regard to claim 55, Hyldig-Nielsen expressly teaches multiple labels (see page 18, where both FITC and carboxyfluorescein are discussed and page 17, where biotin labeling is discussed).

With regard to claims 61 and 62, Hyldig-Nielsen teaches kits for detection which comprise PNA reagents (see page 4, lines 26-30) as well as solid phase reagent systems (see page 27, line 11).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize the PNA backbone of Hyldig-Nielsen in the probes of Shah, Hogan or Britschgi since Hyldig-Nielsen teaches that "The present PNA probes form complexes with complementary nucleic acids which complexes are considerably more stable (higher Tm value) than would be a similar hybrid formed by a typically used nucleic acid probe of corresponding sequence allowing sensitive assays to be made with shorter probes than is the case of typical nucleic acid probes used today. Hybridization with traditionally used nucleic acid probes is much faster in solution than in solid phase hybridization. Due to the high affinity of PNA for nucleic acid, even solid phase hybridization between PNA probes and nucleic acid can be performed rapidly allowing greater flexibility in assay format. Hybridization efficiency is only slightly influenced by pH and salt concentration in the hybridiation solution allowing PNAs to hybridize under conditions not favourable for ordinary DNA probes. Furthermore, PNAs have a higher thermal instability of mismatching bases wehreby PNAs exhibit a greater specificity for their complementary nucleic acids than traditionally used nucleic acid probes of corresponding sequence

would do (ref omitted). The structure of PNA is not degraded by nucleases or proteases making the PNA molecular very stable in biological solutions (page 3, line 21 to page 4, line 7)".

An ordinary practitioner would have been abundantly motivated to utilize the PNA backbone in the mycobacterial probes of Shah, Hogan or Britschgi in order to gain the advantages of improved stability, increased specificity, increased speed of hybridization, increased assay format flexibility, and improved resistance to nucleases which are provided by PNAs.

Allowable Subject Matter

10. Claims drawn and limited to PNAs comprising SEQ ID Nos: 40, 44, 76, 89 and 90 would be novel and unobvious over the cited prior art.

Response to Arguments

11. Applicant's arguments filed July 26, 2002 have been fully considered but they are not persuasive.

Applicant first argues that the invention is distinct because Mycobacteria differ from other bacteria in their cell wall and such probes would be difficult, according to Applicant's argument, to use "ex vivo". This argument is literally not relevant to the claimed invention. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, there is no limitation that the method be performed "within the cell", since the claims are drawn to PNA products, not methods. So the PNA products can be used in the ordinary blotting methods which are taught by Hyldig-Nielsen, such as the ELISA capture assay in example 3 of Hyldig-

Nielsen. This assay does not occur within the cells. With regard to isolation of DNA from Mycobacterial, each of the other primary references, Shah et al (U.S. Patent 5, 521,300) or Hogan et al (U.S. Patent 5,541,308) or Britschgi et al (U.S. Patent 5,726,021), successfully detect Mycobacteria with DNA probes. For example, Hogan expressly, in example 1, detects Mycobacterium by a hybridization reaction using DNA probes. This directly rebuts Applicants incorrect and inaccurate statement that there is any difficulty in detection of Mycobacterial DNA. It is important to recognize that once the DNA is outside of the cell, it is exactly the same, chemically, functionally and biologically, (with due regard for the variation in hybridization and coding functions due to the specific sequence) as any other bacterial DNA, and in fact, as any other DNA from any source, whatsoever.

Applicant then argues that it cannot be assumed that PNA probes will work where DNA and RNA probes work. This statement is flatly contradicted by the statements and evidence provided in Hyldig Nielsen. At page 33, Hyldig-Nielsen compares DNA and PNA and finds that at every concentration, PNA works better than DNA. Hyldig-Nielsen, in example 5, function in a FISH assay to detect every organism.

Applicant then argues this is an "obvious to try" situation. The legal standard for "reasonable expectation of success" is provided by caselaw and is summarized in MPEP 2144.08, which notes "obviousness does not require absolute predictability, only a reasonable expectation of success; i.e. , a reasonable expectation of obtaining similar properties. See , e.g. , In re O'Farrell , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)." In this factual case, there is express showing by Hyldig-Nielsen that PNAs

work better than DNA in hybridization assays in the detection of bacteria nucleic acids. This is sufficient for a reasonable expectation of success. The MPEP cites In re O'Farrell, which notes regarding "obvious to try" at page 1682, that,

> "In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. E.g ., In re Geiger , 815 F.2d at 688, 2 USPQ2d at 1278; Novo Industri A/S v. Travenol Laboratories, Inc ., 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir. 1982); In re Yates , 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); In re Antonie , 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. In re Dow Chemical Co ., 837 F.2d, 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1985); Hybritech, Inc. v. Monoclonal Antibodies, Inc ., 802 F.2d 1367, 1380, 231 USPQ 81, 90-91 (Fed. Cir. 1 986), cert. denied , 107 S.Ct. 1606 (1987); In re Tomlinson ; 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966).

The court in O'Farrell then, affirming the rejection, notes " Neither of these situations applies here." For the instant case, it is clear that neither situations applies here either. This is not a situation where the prior art suggests varying a variety of parameters, since the prior art of Hyldig-Nielsen directly points to the use of PNA for detection of bacteria. This is also not a situation where only general guidance was given. The prior art of Hyldig-Nielsen provides specific guidance directing the use of PNA for detection of bacteria.

Based upon the teachings of Hyldig-Nielsen, the ordinary practitioner would have not only a reasonable expectation of success in detection of Mycobacterial DNA with PNA, but would have an almost complete and 100% expectation of success. The extremely unexpected result would be if the PNA probes did not work.

Applicant then argues that there is evidence of specificity of the probes. As shown in the prior art of Hogan, as well as the other primary references, many probes which are species specific for Mycobacteria are known. If Applicant wishes to rely upon unexpected results for any particular probe, the claim must be commensurate in scope with the unexpected result. Since the current claims are very generic, and are not limited to specific SEQ ID NO: probes, the argument regarding the results is not commensurate in scope with the broad claims.

Conclusion

12. This is a CPA of applicant's earlier Application No. 09/544,934. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634

June 5, 2003